

Evelyne DELFOURNE et al.

R E M A R K S

The above changes in the specification and claims merely place this national phase application in the same condition as it was during Chapter II of the international phase, with the multiple dependencies being removed. Following entry of this amendment only claims 1-13 remain pending in this application. Attached hereto is a marked-up version of the changes made to the specification, claims and abstract by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE".

Respectfully submitted,  
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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

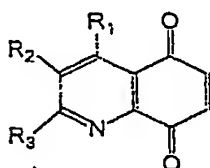
The claims have been amended as follows:

8. ~~(Amended)~~ Pharmaceutical composition comprising an effective amount of a compound selected from the compounds according to ~~any one of Claims 1 to 7~~ ~~Claim 1~~ for treating, by virtue of their cytotoxic properties, cancerous tumours and their metastases.

9. ~~(Amended)~~ Use of the compounds as defined in ~~any one of Claims 1 to 7~~ ~~Claim 1~~ in the manufacture of an anticancer medicament.

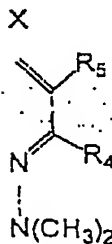
10. (Amended) Process for the preparation of compounds according to Claim 1, which consists in:

a) reacting, according to a hetero Diels-Alder reaction, a quinolinedione of formula:



IV

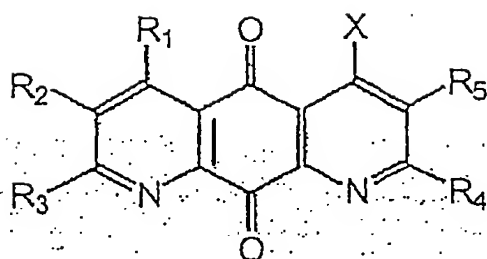
and an azadiene of formula



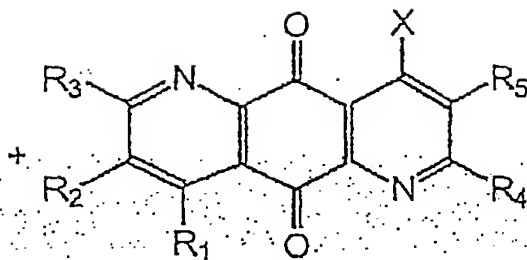
V

where X = CH<sub>3</sub>,

in order to obtain a mixture of compounds



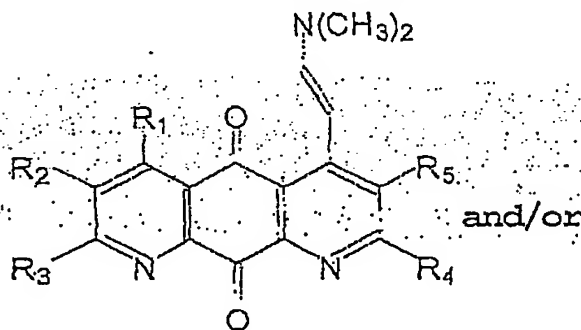
Formula II



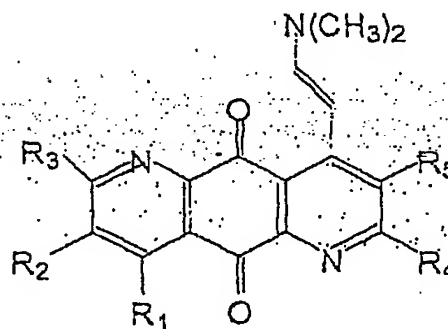
Formula IIa

b) optionally separating the compounds of formulae II and IIa,

c<sub>1</sub>) subsequently reacting a compound of formulae II and or IIa with dimethylformamide dimethyl acetal, in order to obtain an enamine of formula:



Formula III



Formula IIIa

then functionalizing the enamines, in order to introduce the R<sub>6</sub> and/or R<sub>7</sub> substituents, and cyclizing, in order to obtain the compounds of formulae I and/or Ia,

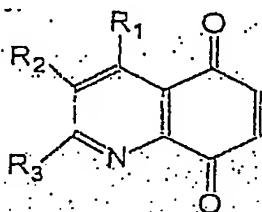
or

c<sub>2</sub>) functionalizing and cyclizing at the same time, in order to obtain the compounds of formulae I and/or Ia,

d) optionally separating the compounds of formulae I and Ia.

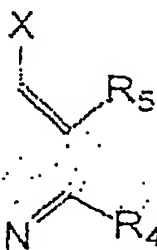
11. (Amended) Process for the preparation of compounds according to Claim 1 of formulae I or Ia in which R6 and R7 are hydrogen atoms, which consists:

a) in reacting, according to a hetero Diels-Alder reaction, a quinolinedione of formula:

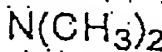


IV

and an azadiene of formula

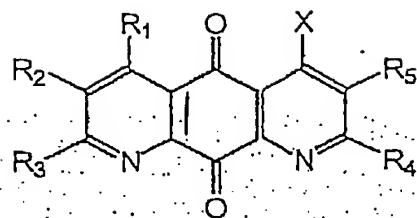


V

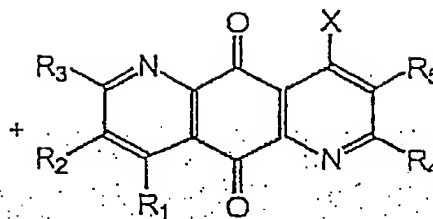


where X = CH<sub>2</sub>-CH<sub>2</sub>-NHBoc,

in order to obtain a mixture of compounds



Formula II



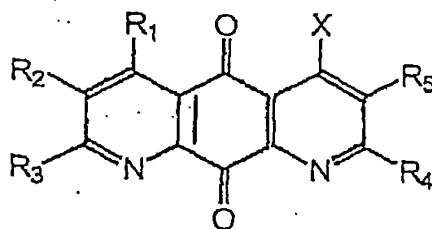
Formula IIa

b) optionally separating the compounds of formulae II and IIa,

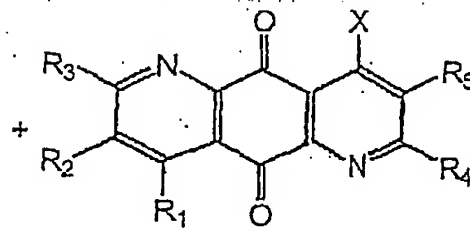
c) cyclizing a compound of formulae II and/or IIa, in order to obtain a compound of formulae I and/or Ia,

d) optionally separating the compounds of formulae I or Ia.

Page 7, Formula II and Formula IIa have been amended as follows:

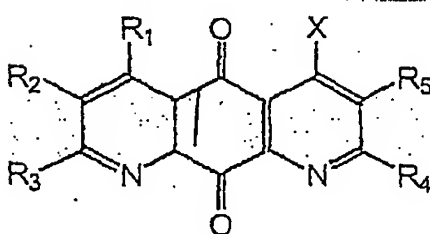


Formula II

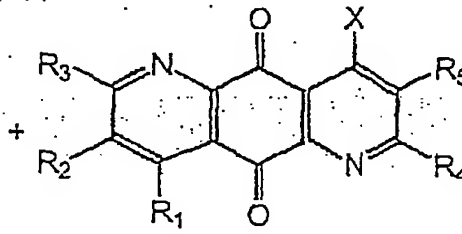


Formula IIa

Page 9, Formula II and Formula IIa have been amended as follows:



Formula II



Formula IIa

The abstract has been amended as follows:

ABSTRACT

~~The invention concerns a~~ pharmaceutical composition comprising ~~including an~~ efficient amount of a compound selected among the compounds of formulae (I) and (Ia), wherein ~~R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> are as defined in Claim 1. Said (Ia).~~ The compounds have interesting cytotoxic properties leading to a therapeutic use as antitumoral medicines.